DEPARTMENT OF ANAESTHESIA & PERIOPERATIVE MEDICINE
UNIVERSITY OF CAPE TOWN

Are you using alpha too?

Procedural analgosedation in the operating theatre

Ross Hofmeyr, Associate Professor, Department of Anaesthesia & Perioperative Medicine, University of Cape Town

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This presentation was developed on request of Pfizer SA, who have provided an honorarium. The presentation has been reviewed and is not been altered in any way from its original form.

Precedex® for use during airway teaching cases was donated to Groote Schuur Hospital by the previous supplier. The speaker does not have any conflicting relationship with either company.

Ross has used quite a lot of Pfizer's other little blue pills while climbing big mountains, but that's another story.

Ross Hofmeyr

MBChB, DipPEC, DA, Mmed, FCA, FAWM

Associate Professor

Director: UCT-Storz Fellowship in Airway & Thoracic Anaesthesia

Department of Anaesthesia & Perioperative Medicine

University of Cape Town

What I'm *not* going to tell you

Off-label uses

Paediatric use

ICU sedation

Applications for agitated delirium

Pfizer Laboratories (Pty) Ltd
Precedex
Approved Package Insert – 30 June 2016

INDICATIONS

PreceDEX is an alpha$_2$ adrenoreceptor agonist sedative with analgesic properties indicated for;

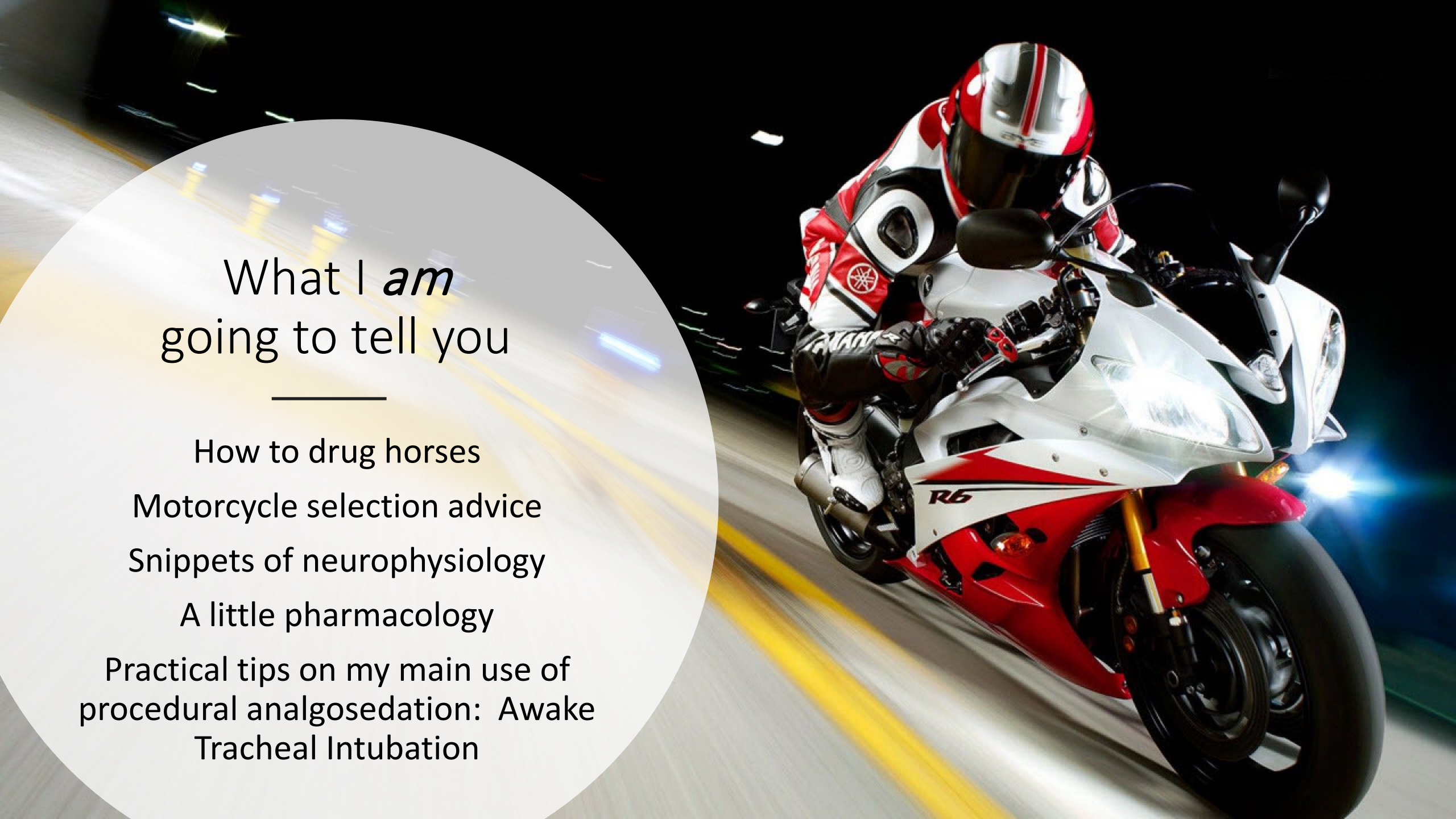
- **Intensive Care Unit Sedation**

Sedation of intubated and mechanically ventilated adult post-surgical patients during treatment in an intensive care setting.

- **Monitored Anaesthesia Care (MAC)/ Conscious sedation in a theatre or intensive care setting for:**
  - Minor surgical procedures under local anaesthesia
  - Fibreoptic intubation

Efficacy and safety has not been studied in children under 18 years of age.

"...should not be used outside an ICU or operating theatre. There should be continuous monitoring or vital parameters"



What I *am* going to tell you

How to drug horses

Motorcycle selection advice

Snippets of neurophysiology

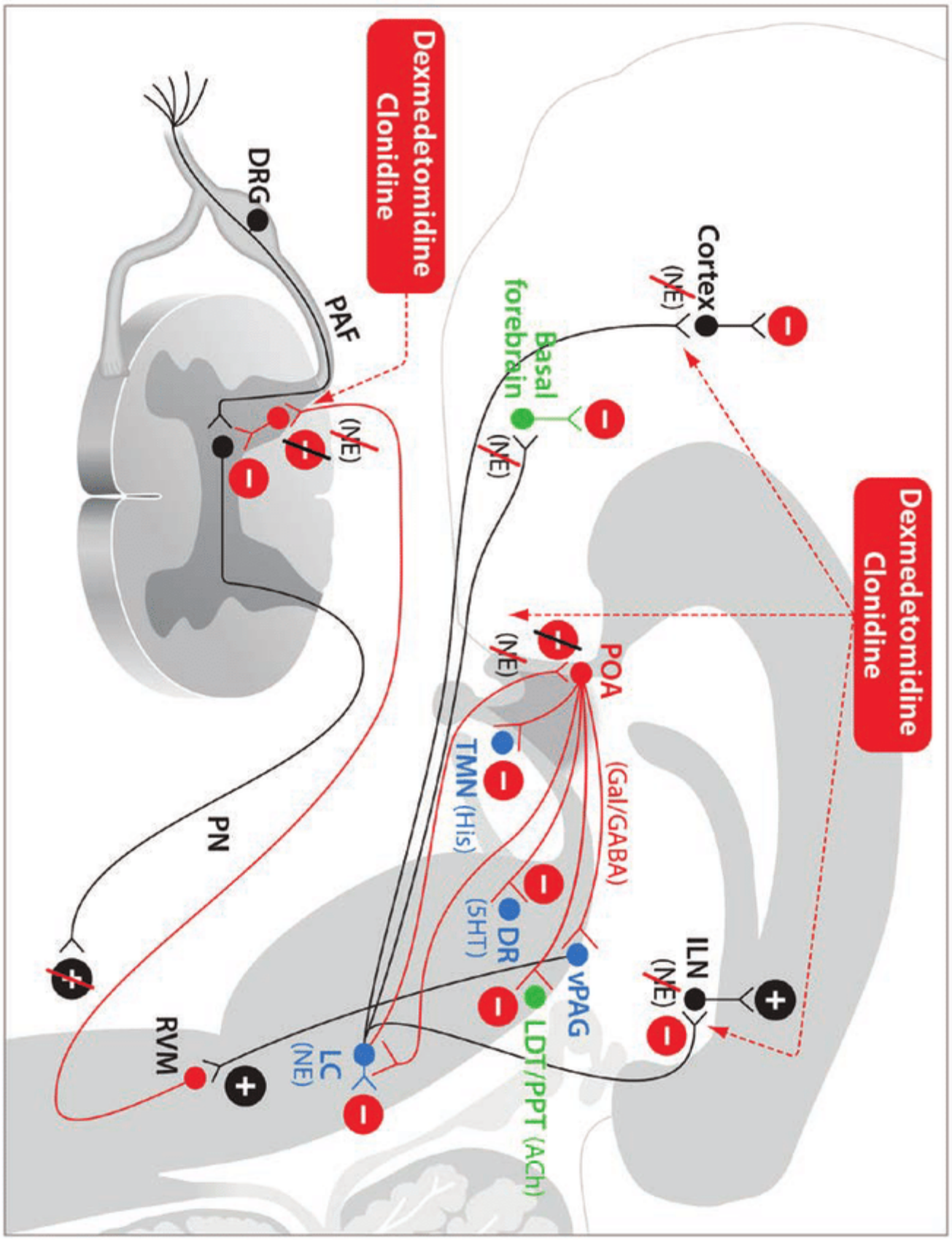
A little pharmacology

Practical tips on my main use of procedural analgosedation: Awake Tracheal Intubation

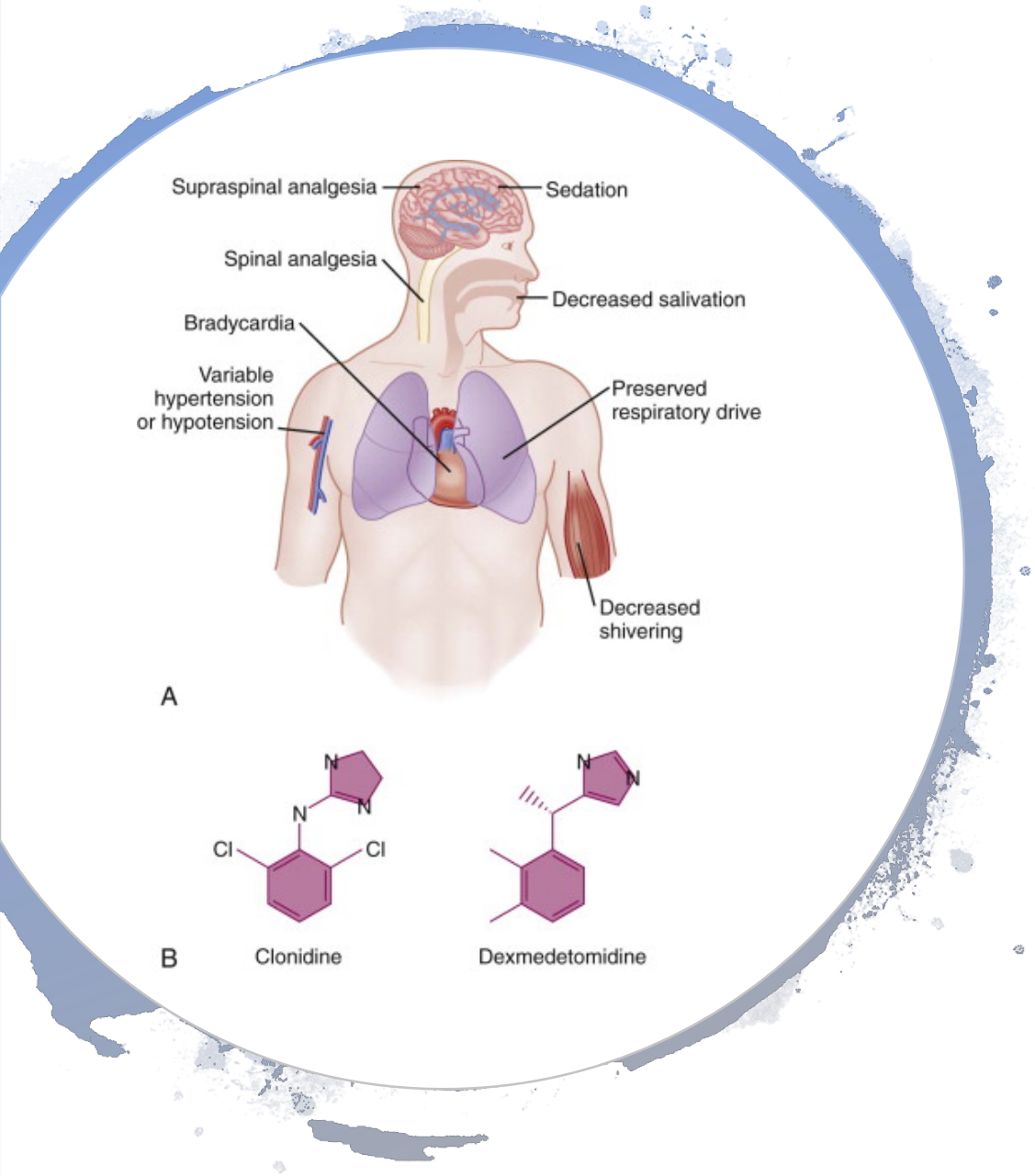
SPECIAL ARTICLE

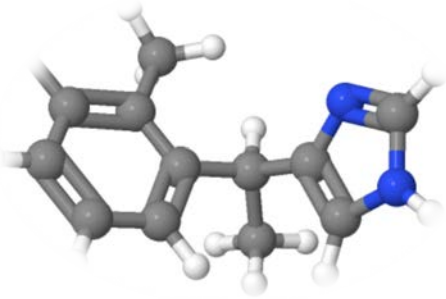
Multimodal General Anesthesia: Theory and Practice

Emery N. Brown, MD, PhD,*†‡§‖ Kara J. Pavone, BS, BSN, RN,* and Marusa Naranjo, MD¶



Dexmedetomidine





Much more highly alpha$_2$ specific than clonidine

Central sedative effect (locus cereleus)

- Alpha$_{2A}$ receptors – upstream of GABA
- Mimics normal sleep
- Less prominent respiratory depression as GABA-ergic agents

Central, spinal cord and peripheral antinociceptive (pre- and post-synaptic alpha$_2$ effect)

No myocardial effects

Transient increase in MAP due to some alpha$_1$ effect

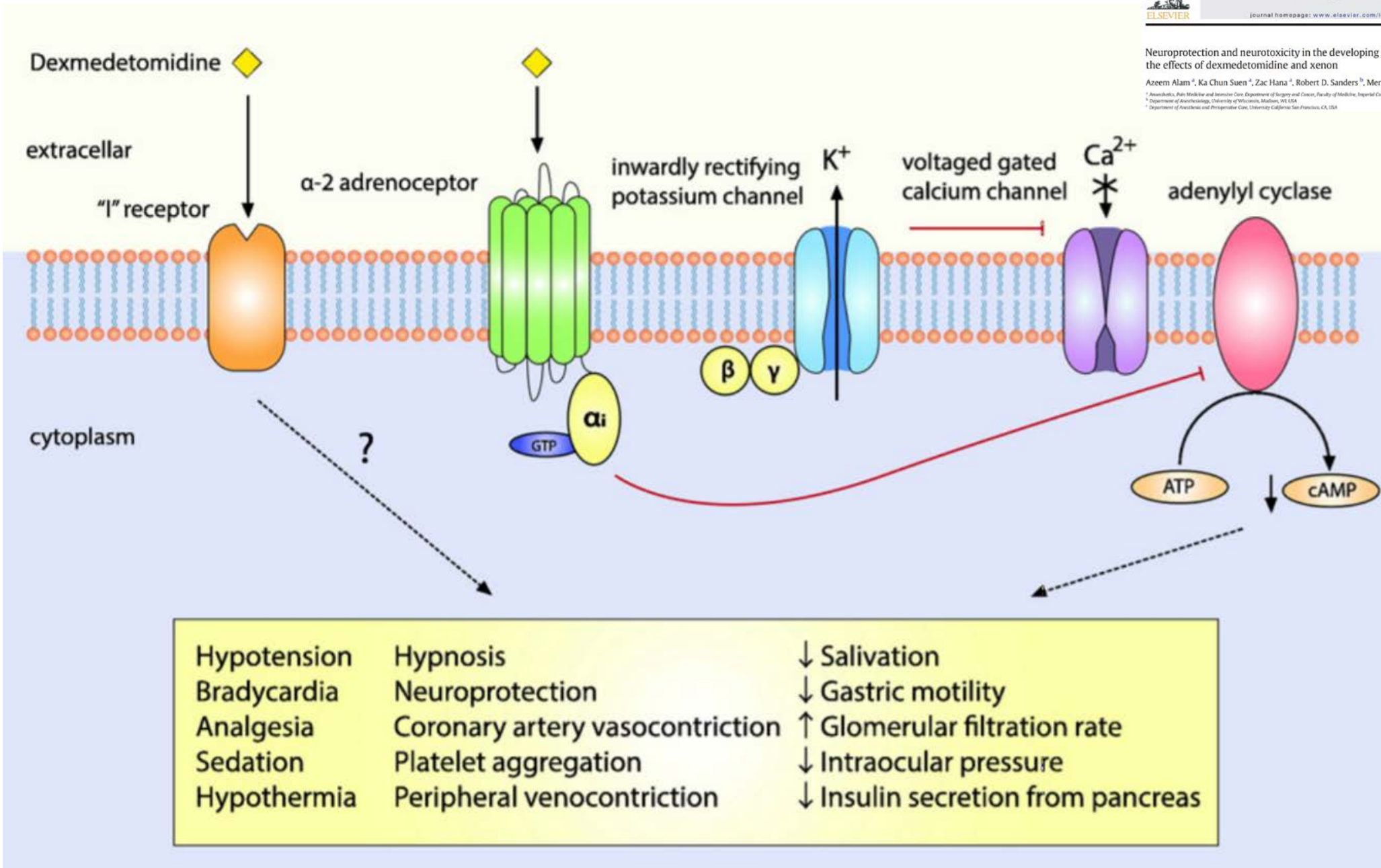
Significant bradycardia and hypotesion due to alpha$_{2A}$

Contents lists available at ScienceDirect
Neurotoxicology and Teratology
journal homepage: www.elsevier.com/locate/neutera

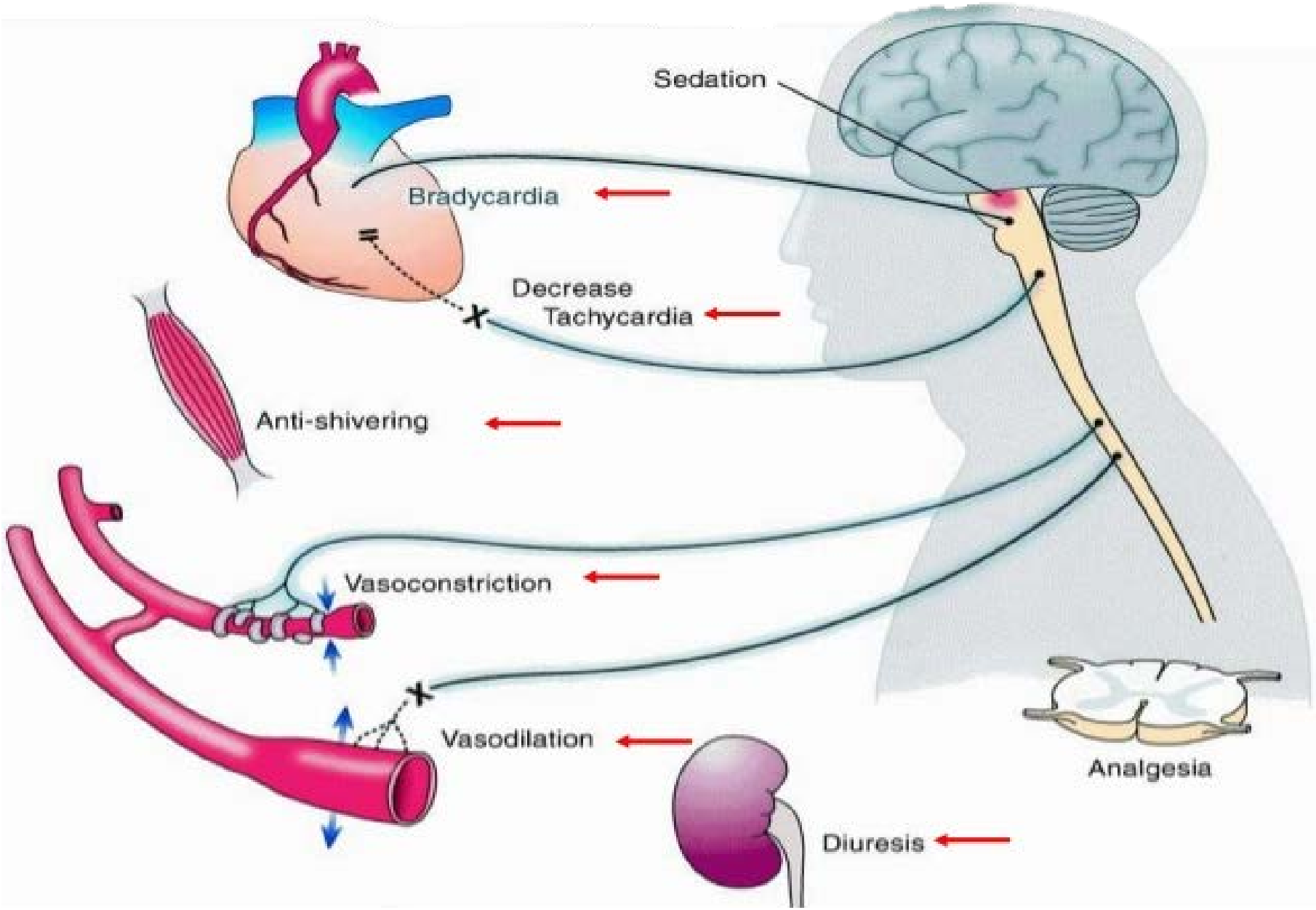
Neuroprotection and neurotoxicity in the developing brain: an update on the effects of dexmedetomidine and xenon

Azeem Alam [a], Ka Chun Suen [a], Zac Hana [a], Robert D. Sanders [b], Mervyn Maze [c], Daqing Ma [a,*]

[a] Anaesthetics, Pain Medicine and Intensive Care, Department of Surgery and Cancer, Faculty of Medicine, Imperial College London, Chelsea & Westminster Hospital, London, UK
[b] Department of Anesthesiology, University of Wisconsin, Madison, WI, USA
[c] Department of Anesthesia and Perioperative Care, University California San Francisco, CA, USA



Hypotension	Hypnosis	↓ Salivation
Bradycardia	Neuroprotection	↓ Gastric motility
Analgesia	Coronary artery vasocontriction	↑ Glomerular filtration rate
Sedation	Platelet aggregation	↓ Intraocular pressure
Hypothermia	Peripheral venocontriction	↓ Insulin secretion from pancreas


Sedation
Bradycardia
Decrease
Tachycardia
Anti-shivering
Vasoconstriction
Vasodilation
Analgesia
Diuresis

Dexmedetomidine action on Alpha2-receptors

Alpha2 A

Anesthesia
Analgesia
Symphatolysis
Sedation
Anxiolysis
Hypnosis
Co-operation

Alpha2 B

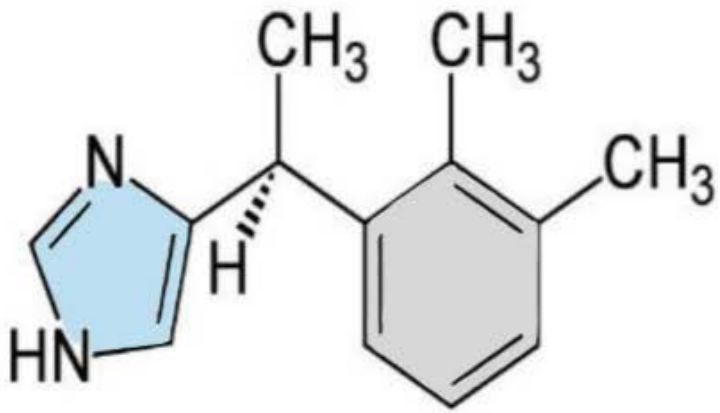
Hypertension

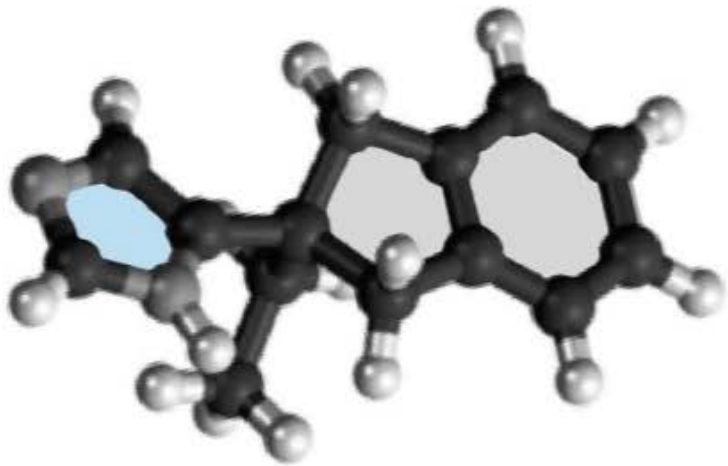
Alpha2 C

Anxiolysis
Drug Withdrawal

Alpha2 D

Unknown





REVIEW ARTICLE

Dexmedetomidine in the Management of Awake Fiberoptic Intubation

Aniello Alfieri[1,*], Maria B. Passavanti[1], Sveva Di Franco[1], Pasquale Sansone[1], Paola Vosa[2], Francesco Coppolino[1], Marco Fiore[1], Caterina Aurilio[1], Maria C. Pace[1] and Vincenzo Pota[1]

[1]*Department of Women, Child and General and Specialized Surgery, University of Campania "Luigi Vanvitelli", Naples, Italy*
[2]*Unit of Pediatric Intensive Care and Neurosurgery. A.O.R.N. Santobono-Pausillipon, Naples, Italy*

Pharmacokinetics

Distribution $t_{1/2}$ 6 minutes

Elimination $t_{1/2}$ 2 hours

Onset ~30 minutes; more rapid with loading dose

Analgesic duration ~4 hours

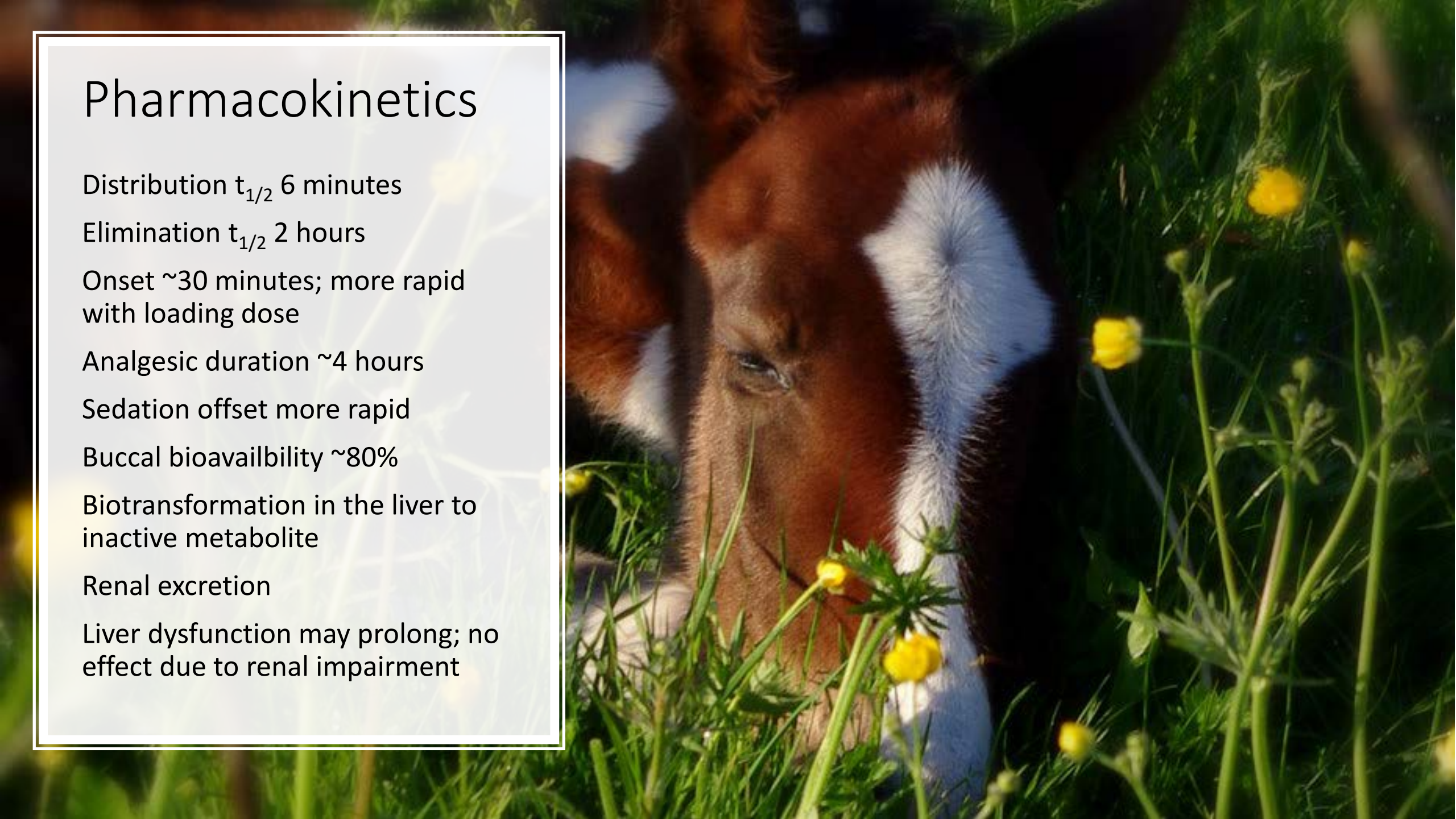
Sedation offset more rapid

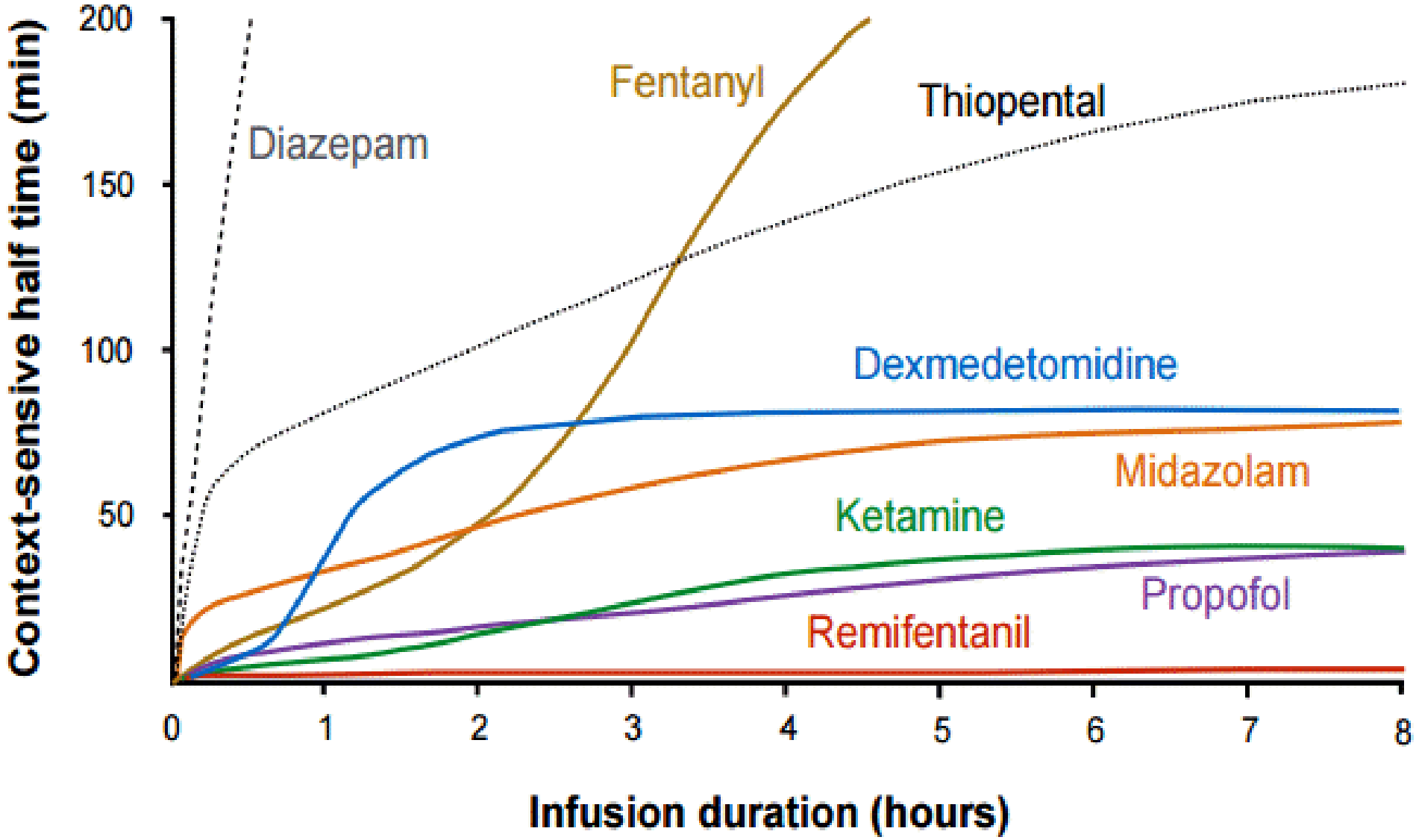
Buccal bioavailbility ~80%

Biotransformation in the liver to inactive metabolite

Renal excretion

Liver dysfunction may prolong; no effect due to renal impairment




Context-sensive half time (min)
200
150
100
50
0
1
2
3
4
5
6
7
8
Infusion duration (hours)
Diazepam
Fentanyl
Thiopental
Dexmedetomidine
Midazolam
Ketamine
Propofol
Remifentanil

ATI: What am I trying to achieve?

Patient comfort

Analgesia

Anxiolysis

Amnesia

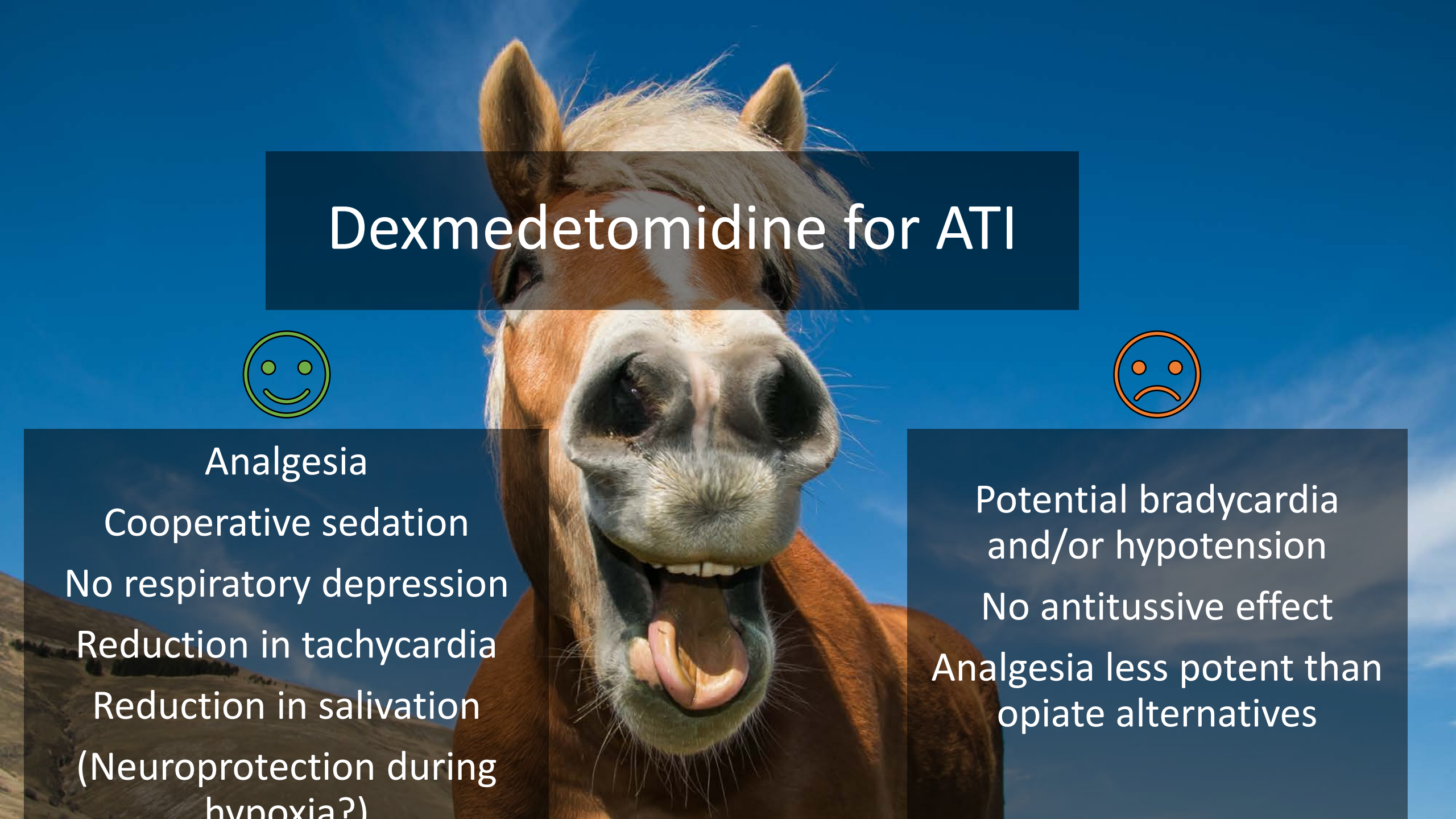
Spontaneous breathing

Reduced coughing

Reduced secretions/salivation

Haemodynamic stability

Dexmedetomidine for ATI



Analgesia

Cooperative sedation

No respiratory depression

Reduction in tachycardia

Reduction in salivation

(Neuroprotection during hypoxia?)

Potential bradycardia and/or hypotension

No antitussive effect

Analgesia less potent than opiate alternatives

The Open Anesthesia Journal

Content list available at: https://openanesthesiajournal.com

REVIEW ARTICLE

Dexmedetomidine in the Management of Awake Fiberoptic Intubation

Aniello Alfieri[1,*], Maria B. Passavanti[1], Sveva Di Franco[1], Pasquale Sansone[1], Paola Vosa[2], Francesco Coppolino[1], Marco Fiore[1], Caterina Aurilio[1], Maria C. Pace[1] and Vincenzo Pota[1]

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Cochrane Library

Cochrane Database of Systematic Reviews

He XY, Cao JP, He Q, Shi XY.
Dexmedetomidine for the management of awake fibreoptic intubation.
Cochrane Database of Systematic Reviews 2014, Issue 1. Art. No.: CD009798.
DOI: 10.1002/14651858.CD009798.pub2.

Dexmedetomidine for the management of awake fibreoptic intubation (Review)

He XY, Cao JP, He Q, Shi XY

Dexmedetomidine is a selective alpha-2-adrenoceptor agonist that can cause sedation, anxiolysis, analgesic sparing, reduced salivary secretion and minimal respiratory depression; this might be beneficial for patients with a difficult or unstable airway undergoing AFOI.

We searched the medical literature until May 2012 and identified four randomized controlled trials involving 211 patients that were appropriate for inclusion in the review. These studies compared dexmedetomidine versus midazolam, fentanyl, propofol or a sodium chloride placebo for patients undergoing AFOI. We reran our search in November 2013, and four studies are awaiting assessment. We will deal with them when we update the review.

Dexmedetomidine significantly reduced patient discomfort during AFOI compared with control groups in two included trials. No significant differences in intubation time, airway obstruction, low oxygen levels or treatment-emergent cardiovascular adverse events were reported during AFOI between the dexmedetomidine group and the control group.

EXPERIMENTAL AND THERAPEUTIC MEDICINE 9: 1259-1264, 2015

Comparison between remifentanil and dexmedetomidine for sedation during modified awake fiberoptic intubation

HUI-HUI LIU[1*], TAO ZHOU[2*], JIAN-QI WEI[1] and WU-HUA MA[1]

Table II. Anesthetic data during the modified AFOI procedure.

Intubation scores	Rem group	Dex group
Cough, 1/2/3/4, n	23/17/4/1[a]	19/16/7/3
Movement, 1/2/3/4, n	23/13/7/2	21/14/7/3
Intubation time, sec	52.0±20.2	50.1±28.3
Drug requirements, μg	137.4±47.6[a]	61.4±15.2
RSS at intubation	2.2±0.7	2.3±0.6
State entropy at intubation	88.1±0.7	89.2±1.1
Rescue requirement for consciousness, n (%)	3 (10.0)	2 (6.7)
Time to tracheal intubation, sec	531.2±7.2[a]	673.1±8.3

Data are expressed as the mean ± standard deviation, or as a number and percentage (n=45). [a]P<0.05, vs. Rem group; AFOI, awake fiberoptic orotracheal intubation; RSS, Ramsay Sedation Scale; Dex, dexmedetomidine; Rem, remifentanil.

Table III. Adverse events in patients receiving Rem or Dex during modified AFOI.

Adverse event	Rem group	Dex group
Airway obstruction score, 1/2/3, n	34/7/4	35/7/3
Hypoxia, n (%)	5 (11.1)	4 (8.9)
Respiratory rate, bpm	12±3.4	11±3.9

Data are expressed as the mean ± standard deviation or as a number and percentage (n=45). Dex, dexmedetomidine; Rem, remifentanil; AFOI, awake fiberoptic orotracheal intubation.

Table IV. Postoperative follow-up data.

Follow-up parameters	Rem group	Dex group
Sore throat, n (%)	10 (22.2)	11 (24.4)
Hoarseness, n (%)	3 (6.7)	2 (4.4)
Satisfaction score (1-4)	2 (1-2)	2 (1-2)
Recall of topical anesthesia, n (%)	40 (88.9)	37 (82.2)
Recall of endoscopy, n (%)	28 (62.2)	26 (57.8)
Recall of intubation, n (%)	14 (31.1)	12 (26.7)

Data are expressed as the median (interquartile range) or as a number and percentage (n=45). Dex, dexmedetomidine; Rem, remifentanil.

Xu *et al. BMC Anesthesiology* (2016) 16:52
DOI 10.1186/s12871-016-0219-9

BMC Anesthesiology

RESEARCH ARTICLE Open Access

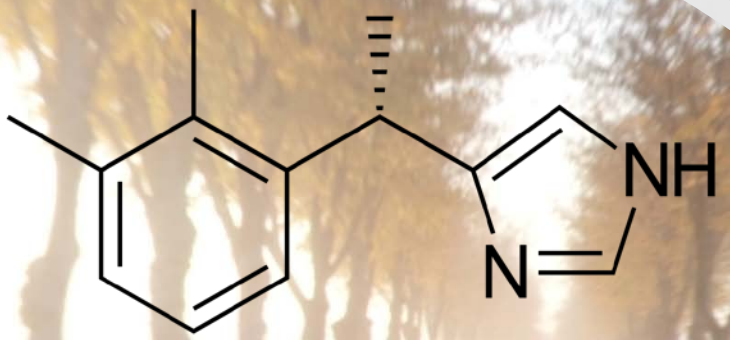
Dexmedetomidine versus remifentanil for sedation during awake intubation using a Shikani optical stylet: a randomized, double-blinded, controlled trial

Ting Xu, Min Li*, Cheng Ni and Xiang-yang Guo

Table 4 Adverse events during airway management

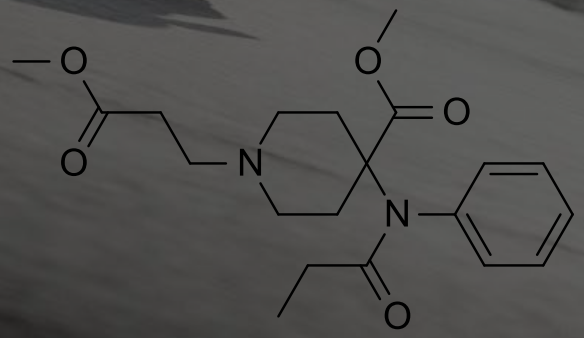
Adverse event	D	R	*P*-value
Hypotension	3 (8.8)	1 (2.9)	0.303
Hypertension	3 (8.8)	6 (17.6)	0.283
Tachycardia	7 (20.6)	9 (26.5)	0.567
Bradycardia	2 (5.9)	0 (0)	0.151
Hypoxia	2 (5.9)	9 (26.5)	0.021
Loosening of teeth	0 (0)	0 (0)	1.000
Injury to lip or oral mucosa	0 (0)	0 (0)	1.000
Postoperative sore throat	16 (47.1)	18 (52.9)	0.628
Hoarseness	2 (5.9)	2 (5.9)	1.000


If you want to go fast, go alone.
If you want to go far, go together.
African Proverb



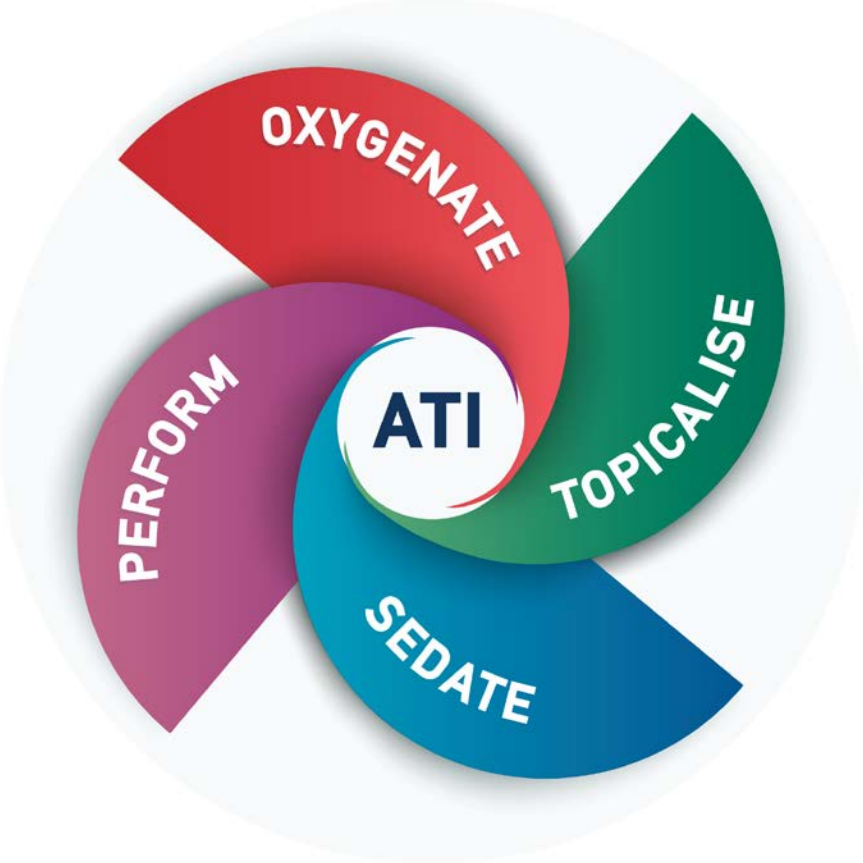
…if you want to go safe, go dex.”

“If you want to go fast, go remi…



Coming soon:

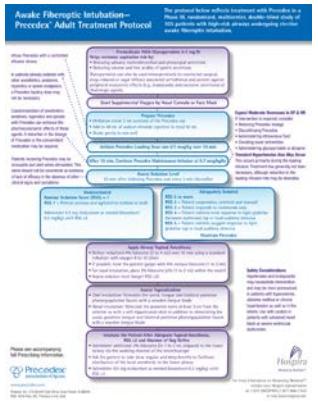
DAS ATI Guidelines



*"**Remifentanil** and **dexmedetomidine** are associated with **high patient satisfaction**, a **low risk of oversedation**, and **low risk of airway obstruction**. A **single agent strategy is safest** for the non-expert, and if used, **remifentanil or dexmedetomidine is advisable (Grade A).** As a sole agent, **propofol is** associated with a greater risk of over-sedation, coughing and airway obstruction than remifentanil, and is therefore **not advisable (Grade A).** If co-administration of agents is to be performed, remifentanil and midazolam are appropriate, recognising the increased risk of over-sedation (Grade E). **Conscious sedation should not be used as a substitute for inadequate airway topicalisation** (Grade E)."*

How I do it…

- Start in good time
- Dexmedetomidine 1 mcg/kg over 15 min
- Nebulise 4% lignocaine during loading
- Continue 0.7 mcg/kg/hr and titrate to effect
- Sitting position
- Atomised lignocaine
- SAYGO
- Induce once ETT visualised in trachea



Awake Fiberoptic Intubation—Precedex® Adult Treatment Protocol

The protocol below reflects treatment with Precedex in a Phase III, randomized, multicenter, double-blind study of 105 patients with high-risk airways undergoing elective awake fiberoptic intubation.

Infuse Precedex with a controlled infusion device.

In patients already sedated with other anesthetics, sedatives, hypnotics or opioid analgesics, a Precedex loading dose may not be necessary.

Coadministration of anesthetics, sedatives, hypnotics and opioids with Precedex can enhance the pharmacodynamic effects of these agents. A reduction in the dosage of Precedex or the concomitant medication may be required.

Patients receiving Precedex may be arousable and alert when stimulated. This alone should not be considered as evidence of lack of efficacy in the absence of other clinical signs and symptoms.

Premedicate With Glycopyrrolate 0.1 mg IV

Helps minimize aspiration risk by:

- Reducing salivary, tracheobronchial and pharyngeal secretions
- Reducing volume and free acidity of gastric secretions

Glycopyrrolate can also be used intraoperatively to counteract surgical, drug-induced or vagal reflexes associated arrhythmias and protect against peripheral muscarinic effects (e.g., bradycardia and excessive secretions) of cholinergic agents.

Start Supplemental Oxygen by Nasal Cannula or Face Mask

Prepare Precedex

- Withdraw entire 2 mL contents of the Precedex vial
- Add to 48 mL of sodium chloride injection to total 50 mL
- Shake gently to mix well

Initiate Precedex Loading Dose one (1) mcg/kg over 10 min

After 10 min, Continue Precedex Maintenance Infusion at 0.7 mcg/kg/hr

Assess Sedation Level

15 min after initiating Precedex and every 3 min thereafter

Expect Moderate Decreases in BP & HR

If intervention is required, consider:

- Reducing Precedex dosage
- Discontinuing Precedex
- Administering intravenous fluid
- Elevating lower extremities
- Administering glycopyrrolate or atropine

Transient Hypertension Also May Occur

This occurs primarily during the loading infusion. Treatment has generally not been necessary, although reduction in the loading infusion rate may be desirable.

Undersedated

Ramsay Sedation Score (RSS) = 1

RSS 1 = Patient anxious and agitated or restless or both

Administer 0.5 mg midazolam as needed (maximum 0.2 mg/kg) until RSS ≥2

Adequately Sedated

RSS 2 or more

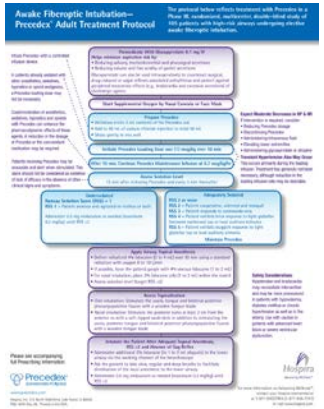
RSS 2 = Patient cooperative, oriented and tranquil

RSS 3 = Patient responds to commands only

RSS 4 = Patient exhibits brisk response to light glabellar (between eyebrows) tap or loud auditory stimulus

RSS 5 = Patient exhibits sluggish response to light glabellar tap or loud auditory stimulus

Maintain Precedex



Apply Airway Topical Anesthesia

- Deliver nebulized 4% lidocaine (2 to 4 mL) over 10 min using a standard nebulizer with oxygen 8 to 10 L/min
- If possible, have the patient gargle with 4% viscous lidocaine (1 to 2 mL)
- For nasal intubation, place 2% lidocaine jelly (1 to 2 mL) within the nostril
- Assess sedation level (target RSS ≥2)

Assess Topicalization

- *Oral intubation:* Stimulate the uvula, tongue and bilateral posterior pharyngopalatine fauces with a wooden tongue blade
- *Nasal intubation:* Stimulate the posterior nares at least 3 cm from the anterior os with a soft-tipped swab stick in addition to stimulating the uvula, posterior tongue and bilateral posterior pharyngopalatine fauces with a wooden tongue blade

Intubate the Patient After Adequate Topical Anesthesia, RSS ≥2 and Absence of Gag Reflex

- Administer additional 2% lidocaine (in 1 to 2 mL aliquots) to the lower airway via the working channel of the bronchoscope
- Ask the patient to take slow, regular and deep breaths to facilitate distribution of the local anesthetic to the lower airway
- Administer 0.5 mg midazolam as needed (maximum 0.2 mg/kg) until RSS ≥2

Safety Considerations

Hypotension and bradycardia may necessitate intervention and may be more pronounced in patients with hypovolemia, diabetes mellitus or chronic hypertension as well as in the elderly. Use with caution in patients with advanced heart block or severe ventricular dysfunction.

Please see accompanying full Prescribing Information.

Precedex®
(dexmedetomidine HCl Injection)

www.precedex.com

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P09-1879-Feb., 09. Printed in the USA.

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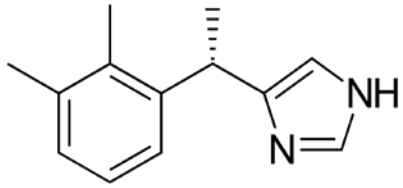
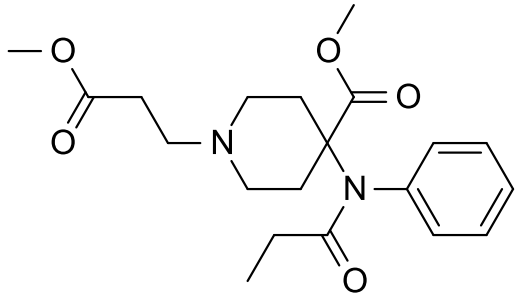
Future directions

DEXMEDETOMIDINE TCI

(DYCK, LIN AND POTTS MODELS)



DEX-REMI COMBINATIONS



Contact me
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Download slides & references
openairway.org/courses-lectures/alpha-too

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